

## **Draft RoC Monograph for Pentachlorophenol: Literature Search Strategy and Preliminary List of References**

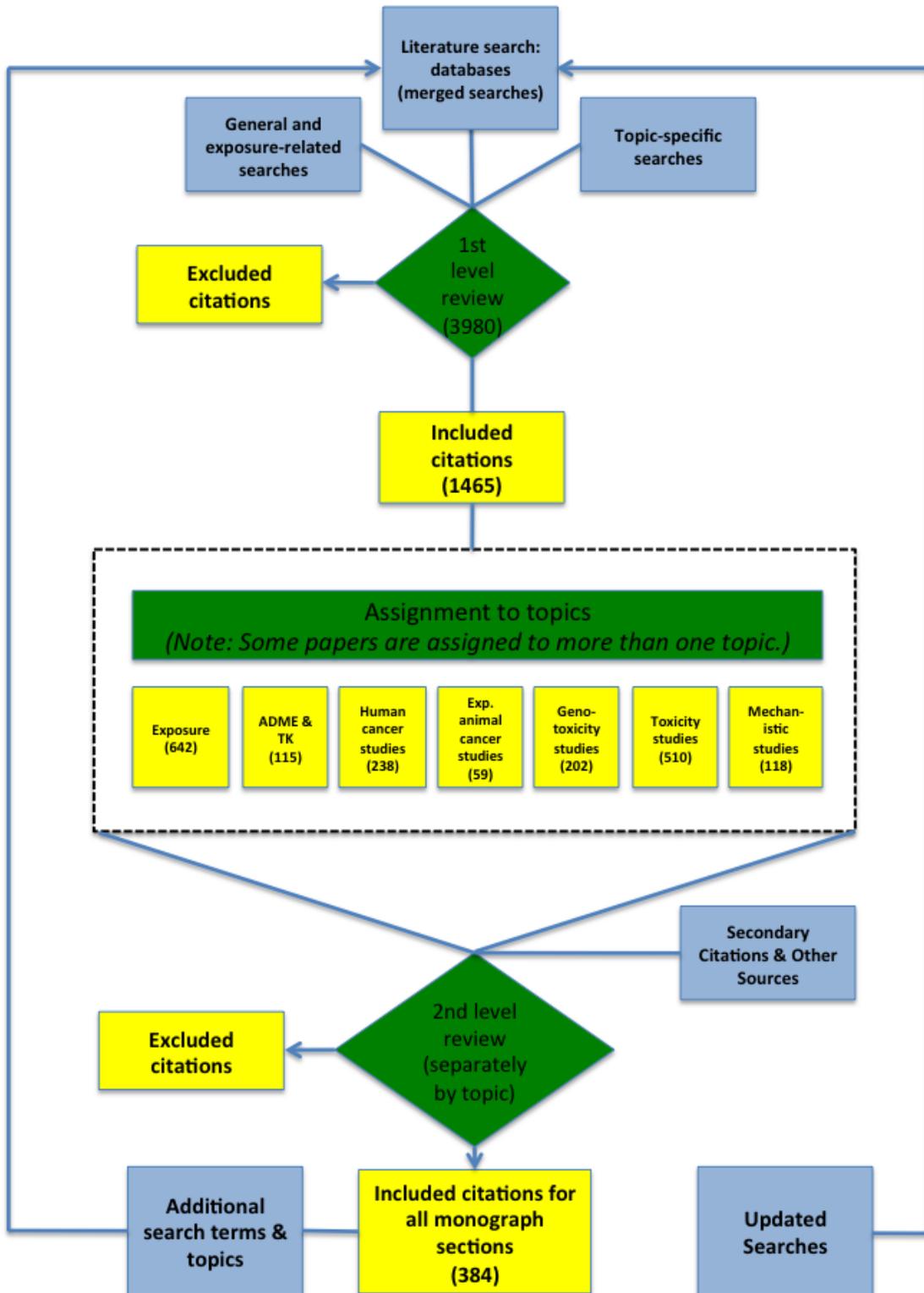
This document describes the data sources, search terms, and search strategies that were used to identify literature for the draft monograph on pentachlorophenol (CASRN 87-86-5). The literature search strategy used for pentachlorophenol involved several approaches designed to identify potentially useful information for the broad range of topics covered by a Report on Carcinogens (RoC) monograph, as listed below.

- Properties and Human Exposure (focusing on the U.S. population)
- Disposition (ADME) and Toxicokinetics
- Human Cancer Studies
- Studies of Cancer in Experimental Animals
- Mechanistic Data and Other Relevant Effects
  - Genetic and Related Effects
  - Mechanistic Considerations

The methods for identifying the relevant literature for the draft pentachlorophenol monograph, including (Part I) the search strategy, (Part II) updating the literature search, and (Part III) the review of citations using web-based systematic review software, are illustrated in Figure 1 and discussed below. Part IV provides information on general searches for by-products of synthesis of pentachlorophenol.

The preliminary list of references used in the preparation of the draft RoC monograph on pentachlorophenol is provided in Part V at the end of this document.

Figure 1. Literature search strategy and review process



## **Part I. Search strategy**

As mentioned in the concept document for pentachlorophenol the specific literature searches are constructed to answer the key questions of the monograph, as a result, not all topic- specific searches will include all the different types of substance- specific search terms; for example, searches for exposure information will only be combined with search terms for pentachlorophenol synonyms since information on exposure to pentachlorophenol metabolites is beyond the scope of this document.

Literature searches in the three databases (see Data Sources, Section 1) are conducted using search terms specific for pentachlorophenol (synonyms, chemical class, metabolites, and exposure scenario) and for the topics covered by the monograph.

Searches for human cancer studies are somewhat unique because they involve the identification of search terms for exposure scenarios in which people may be exposed to pentachlorophenol in addition to search terms specific for pentachlorophenol. For pentachlorophenol, these include terms related to its use as a wood preservative, and in wood- related industries such as sawmills, fencing, and lumber. Because pentachlorophenol was a major pesticide, searches using either pentachlorophenol synonyms or the chemical class should pick up any potential epidemiological studies in the pesticide industry.

In addition to the human cancer studies identified from the above searches, a full- text search for pentachlorophenol is conducted using a QUOSA library of occupational case- control studies.

Relevant literature is identified using search terms, data sources, and strategies as described below.

1. **General data search:** This search covers a broad range of general data sources for information relevant to many or all of the wide range of monograph topics pertaining to pentachlorophenol (see Table 1a,b,c).
2. **Exposure-related data search:** This search covers a broad range of potential sources for exposure-related information and physical-chemical properties (see Table 2).
3. **Database searches in PubMed, Scopus, and Web of Science:** The majority of the primary literature used to draft the pentachlorophenol monograph was identified from searches of these three extensive databases available through the NIEHS Library. Synonyms, metabolites, and the chemical class for pentachlorophenol were identified from the sources listed in Table 3 and the search terms are listed in Table 4. The substance search terms were combined with the search terms for each of the monograph topics listed above to create the specific literature searches. See Table 5 for details on this approach and Table 6 for topic-specific search terms.

Searches for human cancer studies are somewhat unique because they involve the identification of search terms for exposure scenarios that might result in exposure of people to pentachlorophenol. For pentachlorophenol, these exposure-related search terms were based on the manufacture of pentachlorophenol and its use in wood preservation and the use of the handling of the treated wood by workers in sawmills and in fence building; the search terms for those uses were combined with search terms specific for human cancer (see Tables 5 and 6).

4. **QUOSA library of occupational case-control studies** search of the QUOSA-based library of approximately 6,000 occupational case-control studies, approximately 60% of which are currently available as searchable full-text pdfs, was conducted using the synonyms “pentachlorophenol,” “87-86-5 (CASRN),” “hydroxypentachlorobenzene,” “pentachlorobenzene,” “pentachlorophenolate,” “Dowicide EC-7,” and “Dowicide 7.”
5. **Special topic-focused searches:** A topic-specific follow-up search was conducted for pentachlorophenol and immunosuppression using the terms (pentachlorophenol OR hydroxypentachlorobenzene OR pentachlorobenzene OR pentachlorophenolate OR Dowicide) AND (immune AND (system OR suppress\* OR surveillance)) OR (immunosuppress\*).
6. **Secondary sources:** Citations identified from authoritative reviews or from primary references located by literature search, together with publications citing key papers identified using the Web of Science “Cited Reference Search,” were also added.

**General Sources Checklist for: Pentachlorophenol (87-86-5)**

**Table 1a. Comprehensive sources or reviews**

Source	Name of document
1) NTP technical reports	TR349 TR483
2) NTP nomination for toxicological evaluation documents 8/7/2002- ATSDR- PCP 11/0/1976- NCI- PCP, technical 11/0/1976- NCI- Dowicide 8/0/1981- NIOSH- NaPenta CP 7/0/1988- NIEHS- PCP, purified	NF (5 nominations, but no nomination documents)
3) NTP RoC Background Documents	—
4) NTP RoC Profiles	—
5) OHAT (formerly CERHR)	—
6) IARC monographs	Suppl 7 Vol. 53 Vol. 71 Vol. 41 Vol. 20
7) ATSDR Toxicological Profiles	EPA2001 Addendum 2012
8) EPA IRIS	EPA 2010
9) NAS Reports and Publications An Assessment of the Health Risks of Seven Pesticides Used for Termite Control	1 NRC1982
10) WHO (IPCS) INCHEM-related documents (a-k below)	
a) CICADS	—
b) EHC	WHO1987-EHC
c) HSGs	WHO1989- HSG
d) ICSCs	IPCS2003 IPCS2012
e) JECFA	WHO2002-JECFA
f) JMPR	—
g) KemI-Riskline	—
h) PDs	—
i) PIMS	INCHEM1988
j) SIDS	—
k) UKPID	—
11) California EPA Prop 65 hazard identification documents	— (No HID)
12) Health Canada	HC2008 HC2011
13) New York State Department of Health- Health Topics A to Z	

**Table 1b. General information sources**

Source	Name of document
1) U.S. National Library of Medicine (NLM)- TOXNET	
a) HSDB	HSDB2003 (PCP, Na) HSDB2010 (PCP)
b) CCRIS	CCRIS2008
c) GENETOX	GENETOX1991a (PCP, Na)

	GENETOX1991b (PCP, Acetate) GENETOX1991c (PCP)
d) ITER	ITER2010
e) LactMed	NF
f) CPD	CPDB2007
g) CTD	CTD2012
2) PubChem	PubChem2012a (PCP) PubChem2012b (PCP, Na)
3) Kirk-Othmer Encyclopedia- <i>Pentachlorophenol- NF</i> <i>Chlorophenols- Desmurs &amp; Ratton 2000</i> <i>Polyhalogenated Phenols- NF</i> <i>Wood Preservatives- NF</i>	DesmursRatton2000
4) USGS (Minerals	NA

**Table 1c. European Union and other International sources– sources to search**

Source	Name of document
1) International Uniform Chemical Information Database (IUCLID)	—
2) European Chemicals Agency	ECHA2007 CLH2012
3) The International Portal on Food Safety, Animal and Plant Health (IPFSAPH)	EFSA2012 EFSA2009 WTO2008 JMPR1995 JMPR1998 JMPR2003
4) The European Food Safety Authority	—
5) European Centre for Disease Prevention and Control (ECDC)	NA
6) European Monitoring Centre for Drugs and Drug Addiction	NA
7) International Labour Organization (ILO)	ILS2004
8) United Nations Environment Programme (UNEP)	132 hits Saved: CEP1993

**Exposure-Related Sources Checklist for: Pentachlorophenol (87-86-5)**

**Table 2. Exposure- and properties-specific sources**

Source	Name of document
1) U.S. National Library of Medicine (NLM)- TOXNET	
a) ChemIDplus	ChemID2012
b) Haz-Map	HazMap2012a (PCP, Na) HazMap2012b (chlorophenols)
c) HPD	—
d) TOXMAP	TOXMAP2011 (TRI) TOXMAP2009 (Superfund)
2) Akron database	Akron2010a (PCP) Akron2010b (PCP, Na)
3) Chem Sources Suppliers	ChemSources2012
4) National Health and Nutrition Examination Survey (NHANES) data <i>Urinary PCP data identified for 2001–2002 and 2003–2004 NHANES surveys; percent of values in the survey below detection limit document identified.</i>	CDC2009 CDC2011 CDC2013
5) National Occupational Exposure Survey (NOES) (1981–1983)	NIOSH1990
6) National Institute for Occupational Safety and Health (NIOSH) - Hazard Evaluation and Technical Assistance (HETA) reports <i>6 HETA documents identified</i>	Rosensteel 1978 Lee 1986 Lee and Lucas 1983 Gunter and Thoburn 1980 Markel <i>et al.</i> 1977 Markel and Lucas 1975
7) National Response Center (NRC) Database	NRC2012a (Pentachlorophenol – 98) NRC2012b (PCP, Na – 3) NRC2012c (PCP – 19)
8) U.S. International Trade Commission (USITC) Interactive Tariff and Trade DataWeb- Import/Export data	USITC2012
9) EPA Toxics Release Inventory (TRI)	TRI2011 TRI2012
10) Environmental Protection Agency (EPA) AP-42, Compilation of Air Pollutant Emission Factors	—
11) EPA EJView Database	
12) EPA High Production Volume Chemicals (HPV Challenge Program Chemical List)	—
13) EPA Chemical Data Reporting Rule (CDR) (formerly Inventory Update Rule [IUR])	EPA2012
14) EPA Locating and Estimating (L&E) documents	—
15) EPA/Office of Pesticide Programs (OPP) Chemical Ingredients Database	NPIRS2013
16) Food and Drug Administration (FDA) Pesticide Monitoring Database	FDA2008a FDA2008b
17) FDA Orange Book	NA
18) FDA Total Diet Study Not found in 2004-5 market baskets	FDA2006 (1991-3 to 2003- 4 market baskets)
19) Medline Plus	—
20) United States Patent Office <i>48 files identified with “pentachlorophenol” in the patent title</i>	USPTO2013
21) Trademark Electronic Search System (TESS)	—
22) Material Safety Data Sheets (MSDS)- 39 identified	Downloaded:

	Weyerhaeuser1999
23) Dow Chemical Product Safety Assessments	—

**Table 3. Data sources for pentachlorophenol searches**

Information type	Data sources
Synonyms	National Library of Medicine databases (e.g., ChemIDplus, Hazardous Substances Data Base)
Metabolites	EPA (2010), NTP (1999), IARC (1991), Dalhaus <i>et al.</i> (1996)

**Table 4. Literature search approach for pentachlorophenol**

Substance	Search terms	Topics (combined with) <sup>a</sup>
Pentachlorophenol synonyms	Pentachlorophenol, 87-86-5 (CASRN), hydroxypentachlorobenzene, pentachlorobenzene, pentachlorophenate, Dovicide EC-7, Dovicide 7	Human exposure Toxicokinetics Human cancer studies Cancer studies in experimental animals Genotoxicity Toxicity Mechanism
Pentachlorophenol metabolites and their synonyms	tetrachlorophydroquinone (TCHQ), tetrachloro-1,2-hydroquinone (TCoHQ), tetrachlorocatechol (TCpCAT), tetrachloro- <i>p</i> -benzoquinone (TCpBQ), tetrachloro-1,4-benzosemiquinone (TCpSQ), tetrachloro-1,2-benzosemiquinone (TCoSQ), tetrachlorophenol, and trichlorophenol	Human cancer studies Cancer studies in experimental animals (for the mechanistic section) Genotoxicity Toxicity Mechanism
Chemical class synonyms	chlorophenols/chlorinated phenols/polychlorinated phenols	Cancer studies in experimental animals (for the mechanistic section) Genotoxicity Toxicity Mechanism
Exposure scenarios (Dye industry, rubber chemical manufacturing, and herbicide manufacturing)	(wood and preserv*) OR lumber OR sawmill OR fenc*	Human cancer studies

<sup>a</sup> Search terms for each of these topics were developed in consultation with an informational specialist.

**Table 5. Search terms for monograph topics for pentachlorophenol**

Monograph Topic	Search terms used in PubMed, Scopus, and Web of Science	MeSH terms used in Pubmed
Exposure	exposure OR occurrence OR oral OR dermal OR air OR water OR food OR soil OR environmental pollut* OR environmental exposure* OR occupational exposure*	(“Environmental Pollutants” [MeSH] OR “Environmental Pollution” [MeSH])
ADME/ Toxicokinetics	<i>Toxicokinetic search terms-</i> administration OR absorption OR distribution OR tissue distribution OR bioavailab* OR biological availability OR metaboli* OR biotransform* OR activat* OR bioactivat* OR	<i>Toxicokinetic search terms-</i> "Pharmacokinetics"[Mesh] OR "Metabolism"[Mesh] OR "Cytochrome P450

Monograph Topic	Search terms used in PubMed, Scopus, and Web of Science	MeSH terms used in Pubmed
	<p>detoxif* OR excret* OR clearance OR eliminat* OR kinetic* OR pharmacokinetic* OR toxicokinetic* OR cytochrome P450</p> <p><i>Combine with AND</i></p> <p><i>Animal study search terms-</i> in vivo OR animal* OR mouse OR mice OR rat OR hamster OR guinea pig OR rabbit OR monkey OR dog</p>	Enzyme System"[Mesh]
Human Cancer	<p><i>Cancer search terms-</i> cancer OR mortality OR follow-up OR incidence)</p> <p><i>Combine with AND</i></p> <p><i>Epidemiology search terms</i> - epidemiologic* OR workers OR case-control OR cohort OR case-report OR case-series</p>	None
Animal Tumors	<p><i>Cancer search terms-</i> cancer OR neoplasm* OR carcinogen* OR malignan* OR oncogene* OR tumor* OR tumour*</p> <p><i>Combine with AND</i></p> <p><i>Animal study search terms-</i> animal* OR mouse OR mice OR rat OR hamster OR "guinea pig" OR rabbit OR monkey OR dog</p>	<i>Cancer search terms-</i> "Neoplasms"[Mesh]) OR "Carcinogens"[Mesh]
Genotoxicity	<p>genetic toxicology" OR clastogen* OR "DNA strand break*" OR "unscheduled DNA synthesis" OR "UDS" OR aneuploid OR aneuploid* OR polyploid OR polyploid* OR "neoplastic cell transformation" OR "chromosom* aberration*" OR cytogenetic OR cytogenetic* OR "DNA adduct*" OR "DNA damage" OR "DNA repair" OR crosslink* OR "germ-line mutation" OR micronucle* OR mutagen OR mutagen* OR mutation OR mutation* OR oncogen* OR "sister chromatid exchange" OR "SCE" OR "SOS response*" OR "Ames test" OR "gene expression" OR "cell proliferation" OR cytotoxic OR cytotoxic* OR "comet assay"</p>	"DNA Damage"[Mesh] OR "DNA Repair"[Mesh] OR "Mutagens"[Mesh] OR "Mutation"[Mesh] OR "Cytogenetic Analysis"[Mesh] OR "Oncogenes"[Mesh] OR "Mutagenicity Tests"[Mesh]
Toxicity	<p>toxic* OR toxin*OR cytotoxic* OR (nephrotoxic* OR hepatotoxic* OR pneumotoxic* OR thyrotoxic*</p>	"Toxic Actions"[Mesh] OR "Toxicity Tests"[Mesh] OR "adverse effects" [Subheading]
Mechanisms of Carcinogenicity	<p>((mode OR mechanism*) AND action) OR (carcinogen OR genetic OR epigenetic OR inhibit* OR promot* OR interact* OR activate* OR detoxific* OR "oxidative damage" OR alkylat* OR adduct)) AND ((animal OR animals OR mouse OR mice OR</p>	

<b>Monograph Topic</b>	<b>Search terms used in PubMed, Scopus, and Web of Science</b>	<b>MeSH terms used in Pubmed</b>
	rat OR hamster OR "guinea pig" OR rabbit OR monkey OR dog OR pig) OR (person* OR people OR individual* OR subject* OR participant*))	

## **Part II. Updating the literature search**

The literature searches will be updated prior to submitting the draft monograph for peer review and prior to finalizing the monograph. Monthly search alerts for pentachlorophenol synonyms, metabolites, chemical class, exposure scenarios (human cancer), and topic-focused searches were created in PubMed, Scopus, and Web of Science, and the results of these searches from the closing date of the initial search will be downloaded for review.

### **Part III. Review of citations using web-based systematic review software**

Citations retrieved from literature searches were uploaded to web-based systematic review software and screened using inclusion and exclusion criteria. Multi-level reviews of the literature were conducted, with initial reviews (Level 1) based on titles and abstracts only to identify citations that could be excluded and to assign the included literature to one or more monograph topics; subsequent reviews (Level 2) for literature assigned to the various monograph topics (Exposure, ADME & TK, Human cancer studies, etc.) were based on full-text (i.e., PDFs) of the papers and were carried out by the writer and scientific reviewer for each monograph section. Two reviewers, at least one of whom is a member of the OROc at NIEHS, participated at each level of review.

The questions based on inclusion/exclusion criteria for Levels 1 and 2 are listed below.

#### ***Inclusion/exclusion questions for literature***

##### ***Level 1 (Primary screening using titles and abstracts):***

Literature identified from searches in the major databases were categorized in one of three areas-

- 1) General Search (RefIDs 00001-20000)
- 2) Human Cancer Search (RefIDs 20001-40000)
- 3) Animal Tumors Search (RefIDs 40001-60000)

**Note:** In the context of the systematic review of literature used for pentachlorophenol, “relevant information” as it applies to primary screening can include any of the following:

- The article specifically mentions pentachlorophenol, a metabolite, or structural analogue and reports information on one of the topics included in a cancer evaluation (see the list of topics below)
- The article does not specifically mention pentachlorophenol or any related substance, but it does one of the following:
  - It reports information on one of the topics included in a cancer evaluation with potential for exposure to pentachlorophenol and should be included until full-text review, which would provide more information if the study is specific for exposure to pentachlorophenol or a related substance.
  - It reports information on an exposure scenario that could include exposure to pentachlorophenol.
  - It reports information on methodology that is potentially informative for evaluating cancer or mechanistic studies on exposure to pentachlorophenol.
  - It reports information on a potential mode of action that may be informative for pentachlorophenol.

#### **General Search:**

Should we obtain a pdf of this article because it appears to contain potentially relevant information for the review of pentachlorophenol?

- Yes

No

**Human Cancer Search:**

Does this publication appear to contain information on potential exposure to pentachlorophenol (including exposure inferred from knowledge of an exposure scenario) and human cancer? Relevant information includes, but is not limited to, epidemiologic studies, descriptive studies, pooled analyses, meta-analyses, reviews, letters to editors, exposure-assessment studies (for use in epidemiologic studies) and information on co-exposures or potential confounders and other special topics of relevance to the evaluation.

Yes

No

**Cancer in Experimental Animals Search:**

Does this paper potentially contain information on exposure of animals to pentachlorophenol (or to a metabolite, structural analogue, or member of the same chemical class) and the incidence or tumors of the potential for tumor formation (including negative results)?

Yes

No

When “Yes” is selected for any of the questions above, the question below is addressed next:

For which sections of the monograph does the article contain useful information? Check all that apply.

- Properties and Human Exposure
- Toxicokinetics (also includes ADME, i.e., absorption, distribution, metabolism, and excretion)
- Human Cancer Studies
- Studies of Cancer in Experimental Animals
- Mechanisms- Genetic Toxicology
- Mechanisms- Toxicity
- Mechanisms of Carcinogenicity

When “No” is selected for any of the questions above, the next step depends on the category (i.e., general, human, or animal searches).

**General Search:**

Check the reason below that explains the exclusion of this study from further consideration.

It does not contain relevant information on the candidate substance or any related substance (metabolite, structural analogue, or member of the same chemical class).

It contains information relevant to the candidate substance or a related substance (metabolite, structural analogue, or member of the same chemical class), but it does not contain information relevant to any topic covered by the monograph.

Other. (Enter response in text box.)

**Human Cancer Search:**

If the response to Question 1 is “No,” identify all reasons that apply from the list below for excluding this publication from the Human Cancer section.

- Potential exposure to pentachlorophenol is not likely in this study.
- Potential exposure to pentachlorophenol is likely but the study is not a study in humans or related to an issue relevant to interpreting epidemiologic data.
- Other. (Enter response in text box.)

**Cancer in Experimental Animals Search:**

Check the reason below that explains the exclusion of this study from further consideration.

- It does not contain relevant information on the candidate substance or any related substance (metabolite, structural analogue, or member of the same chemical class).
- It contains information relevant to the candidate substance or a related substance (metabolite, structural analogue, or member of the same chemical class), but it does not contain information relevant to any topic covered by the monograph.
- Other. (Enter response in text box.)

*Level 2 (Full text review):*

**Note:** Level 2 reviews exist for all major topics in the monograph, i.e., (1) Exposure, (2) Toxicokinetics (including ADME), (3) Human cancer studies, (4) Animal tumor studies, (5) Genetic toxicology, (6) Toxicity, and (7) Mechanisms of Action. The reviewers for Level 2 topics are asked to consider the following question for all papers:

If this paper could have useful information for any additional sections of the monograph based on your review of the PDF, indicate those additional sections below.

- Properties and Human Exposure
- Toxicokinetics (also includes ADME, i.e., absorption, distribution, metabolism, and excretion)
- Human Cancer Studies
- Studies of Cancer in Experimental Animals
- Mechanisms- Genetic Toxicology
- Mechanisms- Toxicity
- Mechanisms of Carcinogenicity

***Exposure***

1. Does this paper contain information that could be useful in answering the key questions about exposure?
  - Yes
  - No

2. If the answer to Question #1 is “No,” select the reason below for excluding it from review.
- It does not contain relevant information on the candidate substance (or one of its metabolites or analogues).
  - It is related to the candidate substance (or one of its metabolites or analogues), but the paper does not contain information that will help answer the key questions about exposure.
  - Other. (Enter response in text box.)

**Note:** In the context of the systematic review of literature used for pentachlorophenol, “useful information” as it applies to screening for the exposure section can include information, from either primary research papers, review articles, databases, or other published sources, on any of the following topics: occupational exposure, environmental occurrence, occurrence in consumer products, food, cigarette smoke, or other sources, biological indices of exposure, and Federal regulations or guidelines to reduce exposure.

***Toxicokinetics (including Absorption, Distribution, Metabolism, and Excretion)***

1. Does this paper contain information that could be useful in answering the key questions about toxicokinetics?
- Yes
  - No
2. If the answer to Question #1 is “No,” select the reason below for excluding it from review.
- It does not contain relevant information on the candidate substance (or one of its metabolites or analogues).
  - It is related to the candidate substance (or one of its metabolites or analogues), but the paper does not contain information that will help answer the key questions about toxicokinetics.
  - Other. (Enter response in text box.)

**Note:** In the context of the systematic review of literature used for pentachlorophenol, “useful information” as it applies to screening for the toxicokinetics (and ADME) section can include (but is not limited to) information from primary research papers or review articles on any of the following topics: absorption, distribution, metabolism, excretion (ADME), toxicokinetics, and physiologically based pharmacokinetic models (PBPK).

***Human Cancer***

- (1) Does this publication contain relevant information (as defined above) on potential exposure to pentachlorophenol (including exposure inferred from knowledge of an exposure scenario) and human cancer?
- Yes
  - No

**Note:** In the context of the systematic review of literature used for pentachlorophenol, “useful papers” can include (1) cohort studies, (2) case-control studies, (3) case-series studies, or (4) other papers containing useful information. The specific category to which this paper belongs should be indicated in Question #2.

(2) If the answer to Question #1 is “Yes,” what is the study type? (Select all that apply.)

- Cohort study- primary (index) reference
- Cohort study- auxiliary (related) reference
- Case-control study- primary (index) reference
- Case-control study- auxiliary (related) reference
- Case-series study- primary (index) reference
- Case-series study- auxiliary (related) reference
- Other papers directly related to above studies (e.g., letters to the editor, meta-analyses, pooled analyses, etc.)
- Other (e.g., review articles, studies on co-exposures or confounders, etc.)

(3) If the response to Question #1 is “No,” identify all reasons that apply from the list below for excluding this publication from the Human Cancer section.

- (a) No information is provided on potential exposure to pentachlorophenol in this study.
- (b) Potential exposure to pentachlorophenol is likely in the study or is mentioned in the review or publication, but the publication is not one of the following:
  - (i) an epidemiologic study (such as cohort, case-control, ecological, pooled, meta-analysis) or descriptive study (such as case report or case-series) that provides information on human cancer.
  - (ii) a review, letter to the editor, or abstract, or other type of study provided relevant information related to pentachlorophenol and human cancer.
  - (iii) a study or other source of data that provides information, such as on exposure assessment, relevant to evaluating the epidemiologic studies.
- (c) The publication does not provide information on co-exposures or potential confounders or other special topic(s) relevant to the evaluation.

**Note:** In the context of the systematic review of literature used for pentachlorophenol, “useful information” as it applies to screening for the human cancer section can include, but is not limited to, epidemiologic studies, descriptive studies, pooled analyses, meta-analyses, case reports, reviews, letters to editors, exposure-assessment studies (for use in epidemiologic studies) and information on co-exposures or potential confounders and other special topics of relevance to the evaluation.

### *Animal Tumors*

1. Does this paper contain information that could be useful in answering the key questions about animal tumors?

- Yes

No

2. If the answer to Question #1 is “No,” select the reason below for excluding it from review.

It does not contain relevant information on the candidate substance (or one of its metabolites or analogues).

It is related to the candidate substance (or one of its metabolites or analogues), but the paper does not contain information that will help answer the key questions about animal tumors.

Other. (Enter response in text box.)

**Note:** In the context of the systematic review of literature used for pentachlorophenol, “useful information” as it applies to screening for the animal tumors section can include, but is not limited to, information from primary research papers or review articles on (1) chronic studies (ideally for the lifetime of the animal) in experimental animals that are assessing neoplastic endpoints, non-cancer data important for cancer assessment, such as preneoplastic lesions that are considered part of a morphologic continuum to neoplasia, or (2) subchronic studies in experimental animals that provide information on preneoplastic lesions, neoplastic lesions, or on dose setting for chronic studies.

### ***Genetic Toxicology***

1. Does this paper contain information that could be useful in answering the key questions about genetic toxicology?

Yes

No

2. If the answer to Question #1 is “No,” select the reason below for excluding it from review.

It does not contain relevant information on the candidate substance (or one of its metabolites or analogues).

It is related to the candidate substance (or one of its metabolites or analogues), but the paper does not contain information that will help answer the key questions about genetic toxicology.

Other. (Enter response in text box.)

**Note:** In the context of the systematic review of literature used for pentachlorophenol, “useful information” as it applies to screening for the genetic toxicology section can include information from primary research papers or review articles on studies in experimental systems (both *in vitro* and *in vivo*) and in exposed humans assessing the following endpoints: both direct and indirect DNA or chromosomal damage, events associated with mutagenesis, cellular transformation or other related effects.

### ***Toxicity***

1. Does this paper contain information that could be useful in answering the key questions about toxicity?  
 Yes  
 No
2. If the answer to Question #1 is “No,” select the reason below for excluding it from review.  
 It does not contain relevant information on the candidate substance (or one of its metabolites or analogues).  
 It is related to the candidate substance (or one of its metabolites or analogues), but the paper does not contain information that will help answer the key questions about toxicity.  
 Other. (Enter response in text box.)

**Note:** In the context of the systematic review of literature used for pentachlorophenol, “useful information” as it applies to screening for the toxicity section can include any of the following: information from primary research papers or review articles on the toxicity of pentachlorophenol to organs or tissues that were identified as tumor sites from studies in experimental animals.

### ***Mechanistic data***

1. Does this paper contain information that could be useful in answering the key questions about mechanistic data?  
 Yes  
 No
2. If the answer to Question #1 is “No,” select the reason below for excluding it from review.  
 It does not contain relevant information on the candidate substance (or one of its metabolites or analogues).  
 It is related to the candidate substance (or one of its metabolites or analogues), but the paper does not contain information that will help answer the key questions about mechanistic data.  
 Other. (Enter response in text box.)

**Note:** In the context of the systematic review of literature used for pentachlorophenol, “useful information,” as it applies to screening for the mechanistic data section, can include information from primary research papers or review articles on data related to molecular alterations associated with carcinogenicity or potential modes of action, such as genotoxicity, epigenetics, gene expression, immune-response modulation, inflammation, cytotoxicity and compensatory cell proliferation, mitogenicity, chronic metabolic or physiologic overload, nutrient deficiency, and interference with intercellular

communication, for pentachlorophenol, its metabolites and analogues.

#### **Part IV. General searches for by-products of synthesis of pentachlorophenol**

The following by-products of synthesis of pentachlorophenol were identified from NTP Technical Reports 349 and 483:

Dichlorophenol (Table 6a)  
Trichlorophenol (Table 6b)  
Tetrachlorophenol (Table 6c)  
Pentachlorobenzene Table 6d)  
Hexachlorobenzene Table 6e)  
Tetrachlorodibenzodioxin Table 6f)  
Hexachlorodibenzodioxin (Table 6g)  
Heptachlorodibenzodioxin (Table 6h)  
Octachlorodibenzodioxin (Table 6i)  
Pentachlorodibenzofuran (Table 6j)  
Hexachlorodibenzofuran (Table 6k)  
Heptachlorodibenzofuran (Table 6l)  
Octachlorodibenzofuran (Table 6m)  
Heptachlorohydroxydiphenyl ether (No information found)  
Octachlorohydroxydiphenyl ether (No information found)  
Nonachlorohydroxydiphenyl ether (No information found)  
Hexachlorohydroxydibenzofuran (No information found)  
Heptachlorohydroxydibenzofuran (No information found)

The general sources of information, e.g., NTP technical reports, IARC monographs, or ATSDR toxicological profiles, were searched for each of these substances and the results are summarized in Table 6a-m below for each substance.

**Table 6a. General Sources Checklist for: Dichlorophenol**

Source	Name of document
1) NTP technical reports	TR353
2) NTP nomination for toxicological evaluation documents	–
3) NTP RoC Background Documents	–
4) NTP RoC Profiles	–
5) OHAT (formerly CERHR)	–
6) IARC monographs	Volume 71
7) ATSDR Toxicological Profiles	–
8) EPA IRIS	IRIS1987
9) WHO (IPCS) INCHEM-related documents (a-k below)	–
a) CICADS	–
b) EHC	–
c) HSGs	–
d) ICSCs	IPCS2004-2,4-DCP IPCS2004-2,5-DCP IPCS2004-3,5-DCP
e) JECFA	–
f) JMPR	WHO1974-JMPR WHO1975-JMPR
g) KemI-Riskline	–
h) PDs	–
i) PIMS	–
j) SIDS	–
k) UKPID	–
10) California EPA Prop 65 hazard identification documents	–

**Table 6b. General Sources Checklist for: Trichlorophenol**

<b>Source</b>	<b>Name of document</b>
1) NTP technical reports	TR155
2) NTP nomination for toxicological evaluation documents	–
3) NTP RoC Background Documents	–
4) NTP RoC Profiles	3 <sup>rd</sup> RoC
5) OHAT (formerly CERHR)	–
6) IARC monographs	Volume 20 Volume 71 Supplement 4 Supplement 7
7) ATSDR Toxicological Profiles	–
8) EPA IRIS	EPA1987a EPA1987b
9) WHO (IPCS) INCHEM-related documents (a-k below)	–
a) CICADS	–
b) EHC	–
c) HSGs	–
d) ICSCs	IPCS2012-2,3,4-TCP IPCS2012-2,3,5-TCP IPCS2012-2,3,6-TCP
e) JECFA	WHO2002-JECFA
f) JMPR	–
g) KemI-Riskline	–
h) PDs	–
i) PIMS	–
j) SIDS	–
k) UKPID	–
10) California EPA Prop 65 hazard identification documents	–

**Table 6c. General Sources Checklist for: Tetrachlorophenol**

Source	Name of document
1) NTP technical reports	—
2) NTP nomination for toxicological evaluation documents	—
3) NTP RoC Background Documents	—
4) NTP RoC Profiles	—
5) OHAT (formerly CERHR)	—
6) IARC monographs	Volume 71 Supplement 7
7) ATSDR Toxicological Profiles	—
8) EPA IRIS	EPA1987-IRIS
9) WHO (IPCS) INCHEM-related documents (a-k below)	—
a) CICADS	—
b) EHC	—
c) HSGs	—
d) ICSCs	IPCS2012-2,3,4,6-TeCP
e) JECFA	—
f) JMPR	—
g) KemI-Riskline	—
h) PDs	—
i) PIMS	—
j) SIDS	—
k) UKPID	—
10) California EPA Prop 65 hazard identification documents	—

**Table 6d. General Sources Checklist for: Pentachlorobenzene**

<b>Source</b>	<b>Name of document</b>
1) NTP technical reports	TOX006
2) NTP nomination for toxicological evaluation documents	–
3) NTP RoC Background Documents	–
4) NTP RoC Profiles	–
5) OHAT (formerly CERHR)	–
6) IARC monographs	Volume 53 Volume 79
7) ATSDR Toxicological Profiles	–
8) EPA IRIS	EPA1987-IRIS
9) WHO (IPCS) INCHEM-related documents (a-k below)	–
a) CICADS	–
b) EHC	–
c) HSGs	–
d) ICSCs	IPCS2012
e) JECFA	–
f) JMPR	–
g) KemI-Riskline	–
h) PDs	–
i) PIMS	–
j) SIDS	–
k) UKPID	–
10) California EPA Prop 65 hazard identification documents	–

**Table 6e. General Sources Checklist for: Hexachlorobenzene**

Source	Name of document
1) NTP technical reports	–
2) NTP nomination for toxicological evaluation documents	–
3) NTP RoC Background Documents	–
4) NTP RoC Profiles	3 <sup>rd</sup> RoC
5) OHAT (formerly CERHR)	–
6) IARC monographs	Volume 20 Volume 79 Supplement 4 Supplement 7
7) ATSDR Toxicological Profiles	CDC2011-ATSDR
8) EPA IRIS	EPA1988-IRIS
9) WHO (IPCS) INCHEM-related documents (a-k below)	–
a) CICADS	–
b) EHC	WHO1997-EHC
c) HSGs	WHO1998-HSG
d) ICSCs	IPSC2012
e) JECFA	–
f) JMPR	WHO1969-JMPR WHO1973-JMPR WHO1974-JMPR
g) KemI-Riskline	–
h) PDs	WHO-No.26
i) PIMS	INCHEM-PIMS
j) SIDS	–
k) UKPID	–
10) California EPA Prop 65 hazard identification documents	–

**Table 6f. General Sources Checklist for: Tetrachlorodibenzodioxin**

<b>Source</b>	<b>Name of document</b>
1) NTP technical reports	TR201 TR209
2) NTP nomination for toxicological evaluation documents	–
3) NTP RoC Background Documents	–
4) NTP RoC Profiles	2 <sup>nd</sup> RoC
5) OHAT (formerly CERHR)	–
6) IARC monographs	Volume 69 Volume 100f Supplement 7
7) ATSDR Toxicological Profiles	–
8) EPA IRIS	EPA2011-IRIS EPA2012-IRIS
9) WHO (IPCS) INCHEM-related documents (a-k below)	–
a) CICADS	–
b) EHC	–
c) HSGs	–
d) ICSCs	IPCS2012
e) JECFA	WHO2002-JECFA
f) JMPR	–
g) KemI-Riskline	–
h) PDs	–
i) PIMS	–
j) SIDS	–
k) UKPID	–
10) California EPA Prop 65 hazard identification documents	–

**Table 6g. General Sources Checklist for: Hexachlorodibenzodioxin**

<b>Source</b>	<b>Name of document</b>
1) NTP technical reports	TR198 TR2002
2) NTP nomination for toxicological evaluation documents	—
3) NTP RoC Background Documents	—
4) NTP RoC Profiles	—
5) OHAT (formerly CERHR)	—
6) IARC monographs	Volume 53 Volume 69
7) ATSDR Toxicological Profiles	—
8) EPA IRIS	EPA1987-IRIS
9) WHO (IPCS) INCHEM-related documents (a-k below)	—
a) CICADS	—
b) EHC	—
c) HSGs	—
d) ICSCs	—
e) JECFA	WHO2002-JECFA
f) JMPR	—
g) KemI-Riskline	—
h) PDs	—
i) PIMS	—
j) SIDS	—
k) UKPID	—
10) California EPA Prop 65 hazard identification documents	—

**Table 6h. General Sources Checklist for: Heptachlorodibenzodioxin**

Source	Name of document
1) NTP technical reports	–
2) NTP nomination for toxicological evaluation documents	–
3) NTP RoC Background Documents	–
4) NTP RoC Profiles	–
5) OHAT (formerly CERHR)	–
6) IARC monographs	Volume 69
7) ATSDR Toxicological Profiles	–
8) EPA IRIS	–
9) WHO (IPCS) INCHEM-related documents (a-k below)	–
a) CICADS	–
b) EHC	–
c) HSGs	–
d) ICSCs	–
e) JECFA	WHO2002-JECFA
f) JMPR	–
g) KemI-Riskline	–
h) PDs	–
i) PIMS	–
j) SIDS	–
k) UKPID	–
10) California EPA Prop 65 hazard identification documents	–

**Table 6i. General Sources Checklist for:                      Octachlorodibenzodioxin**

<b>Source</b>	<b>Name of document</b>
1) NTP technical reports	—
2) NTP nomination for toxicological evaluation documents	—
3) NTP RoC Background Documents	—
4) NTP RoC Profiles	—
5) OHAT (formerly CERHR)	—
6) IARC monographs	Volume 53
7) ATSDR Toxicological Profiles	—
8) EPA IRIS	—
9) WHO (IPCS) INCHEM-related documents (a-k below)	—
a) CICADS	—
b) EHC	—
c) HSGs	—
d) ICSCs	—
e) JECFA	WHO2002-JECFA
f) JMPR	—
g) KemI-Riskline	—
h) PDs	—
i) PIMS	—
j) SIDS	—
k) UKPID	—
10) California EPA Prop 65 hazard identification documents	—

**Table 6j. General Sources Checklist for:                     Pentachlorodibenzofuran**

<b>Source</b>	<b>Name of document</b>
1) NTP technical reports	TR209-1 TR525 TR526
2) NTP nomination for toxicological evaluation documents	—
3) NTP RoC Background Documents	—
4) NTP RoC Profiles	—
5) OHAT (formerly CERHR)	—
6) IARC monographs	Volume 69 Volume 100F
7) ATSDR Toxicological Profiles	—
8) EPA IRIS	—
9) WHO (IPCS) INCHEM-related documents (a-k below)	—
a) CICADS	—
b) EHC	—
c) HSGs	—
d) ICSCs	—
e) JECFA	WHO2002-JECFA
f) JMPR	—
g) KemI-Riskline	—
h) PDs	—
i) PIMS	—
j) SIDS	—
k) UKPID	—
10) California EPA Prop 65 hazard identification documents	—

**Table 6k. General Sources Checklist for: Hexachlorodibenzofuran**

<b>Source</b>	<b>Name of document</b>
1) NTP technical reports	–
2) NTP nomination for toxicological evaluation documents	–
3) NTP RoC Background Documents	–
4) NTP RoC Profiles	–
5) OHAT (formerly CERHR)	–
6) IARC monographs	Volume 69 Volume 100F
7) ATSDR Toxicological Profiles	–
8) EPA IRIS	–
9) WHO (IPCS) INCHEM-related documents (a-k below)	–
a) CICADS	–
b) EHC	–
c) HSGs	–
d) ICSCs	–
e) JECFA	WHO2002-JECFA
f) JMPR	–
g) KemI-Riskline	–
h) PDs	–
i) PIMS	–
j) SIDS	–
k) UKPID	–
10) California EPA Prop 65 hazard identification documents	–

**Table 6I. General Sources Checklist for: Heptachlorodibenzofuran**

<b>Source</b>	<b>Name of document</b>
1) NTP technical reports	–
2) NTP nomination for toxicological evaluation documents	–
3) NTP RoC Background Documents	–
4) NTP RoC Profiles	–
5) OHAT (formerly CERHR)	–
6) IARC monographs	Volume 69
7) ATSDR Toxicological Profiles	–
8) EPA IRIS	–
9) WHO (IPCS) INCHEM-related documents (a-k below)	–
a) CICADS	–
b) EHC	–
c) HSGs	–
d) ICSCs	–
e) JECFA	WHO2002-JECFA
f) JMPR	–
g) KemI-Riskline	–
h) PDs	–
i) PIMS	–
j) SIDS	–
k) UKPID	–
10) California EPA Prop 65 hazard identification documents	–

**Table 6m. General Sources Checklist for: Octachlorodibenzofuran**

<b>Source</b>	<b>Name of document</b>
1) NTP technical reports	–
2) NTP nomination for toxicological evaluation documents	–
3) NTP RoC Background Documents	–
4) NTP RoC Profiles	–
5) OHAT (formerly CERHR)	–
6) IARC monographs	Volume 69
7) ATSDR Toxicological Profiles	–
8) EPA IRIS	–
9) WHO (IPCS) INCHEM-related documents (a-k below)	–
a) CICADS	–
b) EHC	–
c) HSGs	–
d) ICSCs	–
e) JECFA	WHO2002-JECFA
f) JMPR	–
g) KemI-Riskline	–
h) PDs	–
i) PIMS	–
j) SIDS	–
k) UKPID	–
10) California EPA Prop 65 hazard identification documents	–

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